

ESM Table 1. Baseline characteristics according to the tertiles of relative leucocyte telomere length.

Baseline variables	T1≤4.20	4.20<T2≤5.13	T3>5.13	P value
Number	1362	1361	1362	
Age, year	56.02 ± 12.48	53.90 ± 12.91	52.94 ± 12.24	<0.001
Male, %	631 (46.3%)	612 (45.0%)	610 (44.8%)	0.419
Duration of diabetes, year	6.71 ± 6.14	5.99 ± 6.12	5.44 ± 5.95	<0.001
Current smoker, %	190 (14.0%)	209 (15.4%)	198 (14.6%)	0.653
Ever smoked, %	433 (31.8%)	388 (28.6%)	375 (27.6%)	0.016
Current drinker, %	125 (9.2%)	123 (9.1%)	165 (12.2%)	0.011
Ever drinker, %	303 (22.4%)	268 (19.8%)	289 (21.4%)	0.510
SBP, mmHg	134.83 ± 20.17	131.51 ± 18.92	130.59 ± 18.68	<0.001
DBP, mmHg	76.81 ± 11.00	75.63 ± 10.52	75.44 ± 10.06	0.001
BMI, kg/m ²	25.13 ± 3.89	25.36 ± 4.16	25.36 ± 4.25	0.139
HbA _{1c} , mmol	61.69 ± 20.35	59.57 ± 19.74	57.80 ± 18.89	<0.001
HbA _{1c} , %	7.79 ± 1.86	7.60 ± 1.81	7.44 ± 1.73	<0.001
FPG, mmol/l	8.97 ± 3.31	8.65 ± 3.31	8.32 ± 3.23	<0.001
TC, mmol/l	5.28 ± 1.11	5.09 ± 1.13	5.08 ± 1.10	<0.001
HDL-C, mmol/l	1.31 ± 0.38	1.33 ± 0.38	1.36 ± 0.40	0.001
LDL-C, mmol/l	3.24 ± 0.99	3.02 ± 0.92	2.98 ± 0.93	<0.001
Triacylglycerol, mmol/l	1.33 [0.91, 2.02]	1.30 [0.90, 1.90]	1.35 [0.95, 1.97]	0.956*
Urinary ACR, mg/mmol	1.94 [0.83, 8.15]	1.49 [0.65, 5.24]	1.37 [0.68, 4.25]	<0.001*
eGFR, ml min ⁻¹ 1.73 m ⁻²	89.66 ± 17.00	90.78 ± 17.02	91.77 ± 16.46	0.001
RBC, 10 ¹² /l	4.71 ± 0.57	4.71 ± 0.56	4.77 ± 0.59	0.030
HB, g/l	13.94 ± 1.50	13.91 ± 1.51	13.98 ± 1.50	0.513
WBC, 10 ⁹ /l	7.35 ± 4.07	7.17 ± 1.86	7.08 ± 1.88	0.021
Diagnosed comorbidity				
Retinopathy, %	343 (25.2%)	303 (22.3%)	295 (21.7%)	0.029
Neuropathy, %	293 (21.5%)	232 (17.0%)	157 (11.5%)	<0.001
Microalbuminuria, %	387 (29.2%)	320 (24.4%)	311 (23.7%)	0.001
Macroalbuminuria, %	165 (12.5%)	126 (9.6%)	97 (7.4%)	<0.001
Use of medications				
Lipid lowering drugs, %	171 (12.6%)	213 (15.7%)	245 (18.0%)	<0.001
Antihypertensive drugs, %	539 (39.6%)	523 (38.4%)	514 (37.7%)	0.325
Oral antihyperglycemic drugs, %	875 (64.2%)	925 (68.0%)	952 (69.9%)	0.002
Insulin use, %	191 (14.0%)	180 (13.2%)	164 (12.0%)	0.125
RAS inhibitors (ACEIs or ARBs), %	244 (17.9%)	220 (16.2%)	236 (17.3%)	0.684

All data are shown as mean ± SD, median (Q1-Q3) or proportion in %; All comparisons of clinical characteristics was conducted by using linear regression for continuous variables and logistic regression for category variables with/without adjustment for age; *logarithmic

transformation was used in TG and ACR. A one-unit increase in $\log(\text{TG})$ or $\log(\text{ACR}+1)$ corresponds to a 10-fold increase in TG, or (ACR+1), respectively.

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA_{1c}, Haemoglobin A1c; FPG, fasting plasma glucose; TC, total cholesterol; TG, triacylglycerol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; ACR, urinary albumin to creatinine ratio; RAS inhibitors, renin angiotensin system inhibitors; ACEIs, angiotensin converting enzyme inhibitors; ARBs, angiotensin receptor blockers. T1, tertile 1; T2, tertile 2, T3, tertile 3.

ESM Table 2. Cox regression analysis of the association between shorter rLTL and incident end stage kidney disease in subgroups

ESKD	Events/Total (%)	Hazard Ratio (95% CI)		
		Unadjusted model	Fully adjusted model	<i>p value</i> *
Overall	564/4085 (13.8%)	1.21 (1.13-1.30)	1.11 (1.03-1.19)	0.007
Males	263/1853 (14.2%)	1.18 (1.07-1.31)	1.07 (0.95-1.21)	0.240
Females	301/2232 (13.5%)	1.24 (1.13-1.36)	1.11 (1.01-1.22)	0.025
Age at diagnosis of diabetes				
< 40 years	107/1017 (10.5%)	1.19 (1.01-1.40)	1.24 (1.03-1.49)	0.026
40+ years	457/3067 (14.9%)	1.20 (1.11-1.29)	1.09 (1.00-1.18)	0.039

rLTL, relative leucocyte telomere length calculated by negative control (water); ESKD, end stage kidney disease. * P value for fully adjusted model; Full adjusted model included age, sex, duration of diabetes, BMI, SBP, DBP, HbA_{1c}, LDL-C, Log (TG), HDL-C, eGFR, Log (ACR), retinopathy, neuropathy and CVD at baseline. Sex and retinopathy were included as strata variables.

ESM Table 3 Competing Risk Regression analysis showing subdistribution HRs of rLTL for incident end stage kidney disease.

Subdistribution HRs	rLTL (each unit decrease) sHR	<i>p value</i>
Model 1	1.19 (1.11-1.26)	<0.001
Model 2	1.14 (1.07-1.22)	<0.001
Model 3	1.12 (1.06-1.19)	<0.001
Model 4	1.10 (1.02-1.18)	0.009
Model 5	1.10 (1.02-1.18)	0.009

sHR, subdistribution hazards ratio; rLTL, relative leucocyte telomere length calculated by negative control (water).

Sex and retinopathy were included as strata variables.

Model 1: without adjustment

Model 2: adjusted for age and sex

Model 3: Model 2 + adjusted for duration of diabetes, BMI, SBP and DBP

Model 4: Model 3 + adjusted for HbA1c, LDL-C, log₁₀ (triacylglycerol), HDL-C, eGFR and log₁₀ (ACR)

Model 5: Model 4 + retinopathy, neuropathy and CVD at baseline.

ESM Table 4 Hazard ratio (95% CI) for incident end stage kidney disease according to tertiles (T) of rLTL

Variables	Model 1		Model 2		Model 3		Model 4		Model 5	
	HR (95%CI)	<i>p</i> value	HR (95%CI)	<i>p</i> value	HR (95%CI)	<i>p</i> value	HR (95%CI)	<i>p</i> value	HR (95%CI)	<i>p</i> value
T1 (rLTL≤4.20)	1.77 (1.43-2.19)	<0.001	1.56 (1.26-1.93)	<0.001	1.48 (1.19-1.83)	<0.001	1.41 (1.12-1.78)	0.003	1.39 (1.10-1.75)	0.006
T2 (4.20<rLTL≤5.13)	1.28 (1.02-1.60)	0.032	1.22 (0.97-1.53)	0.085	1.19 (0.95-1.50)	0.127	1.19 (0.93-1.51)	0.169	1.17 (0.92-1.49)	0.210
T3 (rLTL>5.13)	Reference									
Age, years			1.04 (1.03-1.04)	<0.001	1.02 (1.01-1.03)	<0.001	1.00 (0.99-1.02)	0.526	1.01 (0.99-1.02)	0.349
Diabetes duration, years					1.04 (1.03-1.05)	<0.001	1.01 (1.00-1.02)	0.169	1.00 (0.99-1.02)	0.883
BMI, kg/m ²					1.02 (0.99-1.04)	0.194	0.99 (0.97-1.01)	0.368	0.99 (0.97-1.02)	0.508
SBP, mmHg					1.02 (1.02-1.03)	<0.001	1.01 (1.01-1.02)	<0.001	1.01 (1.01-1.02)	<0.001
DBP, mmHg					0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001	0.98 (0.97-0.99)	<0.001
HbA _{1c} , mmol/mol							1.01 (1.01-1.02)	<0.001	1.01 (1.01-1.02)	<0.001
LDL-C, mmol/l							0.86 (0.78-0.94)	0.001	0.85 (0.77-0.93)	0.001
Log (TG)							1.39 (0.90-2.16)	0.142	1.49 (0.96-2.32)	0.075
HDL-C, mmol/l							1.22 (0.95-1.56)	0.113	1.24 (0.97-1.57)	0.088
eGFR, ml min ⁻¹ 1.73 m ⁻²							0.98 (0.97-0.98)	<0.001	0.98 (0.97-0.98)	<0.001
Log (ACR)							3.20 (2.80-3.65)	<0.001	2.92 (2.54-3.36)	<0.001
Neuropathy									1.18 (0.96-1.45)	0.119
CVD at baseline									0.88 (0.67-1.16)	0.355

HR, hazard ratio; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA_{1c}, Haemoglobin A_{1c}; LDL-C, low-density lipoprotein cholesterol; TG, triacylglycerol; HDL-C, high-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; ACR, urinary albumin to creatinine ratio; rLTL, relative leucocyte telomere length calculated by negative control (water)

Sex and retinopathy were included as strata variables.

Model 1: without adjustment

Model 2: adjusted for age and sex

Model 3: Model 2 + adjusted for duration of diabetes, BMI, SBP and DBP

Model 4: Model 3 + adjusted for HbA_{1c}, LDL-C, log₁₀ (triacylglycerol), HDL-C, eGFR and log₁₀ (ACR)

Model 5: Model 4 + retinopathy, neuropathy and CVD at baseline.

ESM Table 5 Linear regression analysis of the association between rLTL and eGFR change during follow-up period.

Variables	Model 1		Model 2		Model 3		Model 4		Model 5	
	Beta ± SE	<i>p</i> value	Beta ± SE	<i>p</i> value	Beta ± SE	<i>p</i> value	Beta ± SE	<i>p</i> value	Beta ± SE	<i>p</i> value
Intercept	-5.25 ± 0.32	<0.001	-1.28 ± 0.49	0.009	2.01 ± 0.86	0.019	0.65 ± 1.31	0.620	0.62 ± 1.30	0.634
rLTL, ΔΔCt	0.42 ± 0.07	<0.001	0.35 ± 0.07	<0.001	0.27 ± 0.06	<0.001	0.14 ± 0.06	0.021	0.13 ± 0.06	0.029
Age, years			-0.06 ± 0.01	<0.001	-0.02 ± 0.01	0.006	-0.01 ± 0.01	0.121	-0.01 ± 0.01	0.146
Male			-0.37 ± 0.16	0.019	-0.60 ± 0.16	<0.001	-0.52 ± 0.15	0.001	-0.48 ± 0.15	0.002
Diabetes duration, years					-0.11 ± 0.01	<0.001	-0.04 ± 0.01	0.003	-0.02 ± 0.01	0.144
BMI, kg/m ²					0.00 ± 0.02	0.836	0.03 ± 0.02	0.071	0.03 ± 0.02	0.116
SBP, mmHg					-0.05 ± 0.01	<0.001	-0.03 ± 0.01	<0.001	-0.03 ± 0.01	<0.001
DBP, mmHg					0.03 ± 0.01	0.006	0.04 ± 0.01	<0.001	0.04 ± 0.01	<0.001
HbA1c, mmol/mol							-0.030 ± 0.004	<0.001	-0.029 ± 0.004	<0.001
LDL-C, mmol/l							-0.04 ± 0.08	0.655	-0.03 ± 0.08	0.710
Log (TG)							-0.40 ± 0.36	0.269	-0.56 ± 0.36	0.119
HDL-C, mmol/l							0.03 ± 0.21	0.873	0.01 ± 0.21	0.980
eGFR, ml min ⁻¹ 1.73 m ⁻²							0.01 ± 0.01	0.019	0.01 ± 0.01	0.050
Log (ACR)							-3.86 ± 0.15	<0.001	-3.67 ± 0.15	<0.001
Retinopathy									-1.07 ± 0.18	<0.001
Neuropathy									-0.65 ± 0.20	0.001
CVD at baseline									0.11 ± 0.24	0.655

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA_{1c}, Haemoglobin A1c; LDL-C, low-density lipoprotein cholesterol; TG, triacylglycerol; HDL-C, high-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; ACR, urinary albumin to creatinine ratio; rLTL, relative leucocyte telomere length calculated by negative control (water)

Model 1: without adjustment

Model 2: adjusted for age and sex

Model 3: Model 2 + adjusted for duration of diabetes, BMI, SBP and DBP

Model 4: Model 3 + adjusted for HbA_{1c}, LDL-C, log₁₀ (triacylglycerol), HDL-C, eGFR and log₁₀ (ACR)

Model 5: Model 4 + retinopathy, neuropathy and CVD at baseline.

ESM Table 6 Sensitivity analysis after excluding incident ESKD defined within 30 days of AKI diagnosis.

Variables	Model 1		Model 2		Model 3		Model 4		Model 5	
	HR (95%CI)	<i>p</i> value	HR (95%CI)	<i>p</i> value	HR (95%CI)	<i>p</i> value	HR (95%CI)	<i>p</i> value	HR (95%CI)	<i>p</i> value
rLTL, $\Delta\Delta\text{Ct}$	1.17 (1.08-1.27)	<0.001	1.13 (1.04-1.22)	0.004	1.11 (1.03-1.20)	0.01	1.09 (1.00-1.19)	0.047	1.09 (1.00-1.19)	0.052
Age, years			1.03 (1.03-1.04)	<0.001	1.02 (1.03)	<0.001	1.00 (0.99-1.02)	0.749	1.00 (0.99-1.01)	0.849
Diabetes duration, years					1.03 (1.05)	<0.001	1.01 (1.03)	0.314	1.01 (1.03)	0.35
BMI, kg/m ²					1.01 (1.04)	0.348	0.99 (1.01)	0.336	0.99 (1.01)	0.338
SBP, mmHg					1.02 (1.03)	<0.001	1.01 (1.02)	0.004	1.01 (1.02)	0.004
DBP, mmHg					0.99 (1.00)	0.021	0.98 (0.99)	0.003	0.98 (0.99)	0.004
HbA _{1c} , mmol/mol							1.01 (1.02)	<0.001	1.01 (1.02)	<0.001
LDL-C, mmol/l							0.83 (0.92)	0.001	0.82 (0.92)	0.001
Log (TG)							1.43 (2.39)	0.17	1.46 (2.45)	0.149
HDL-C, mmol/l							1.17 (1.55)	0.287	1.18 (1.56)	0.261
eGFR, ml min ⁻¹ 1.73 m ⁻²							0.98 (0.98)	<0.001	0.98 (0.98)	<0.001
Log (ACR)							3.49 (4.10)	<0.001	3.42 (4.03)	<0.001
Neuropathy									1.19 (1.52)	0.168
CVD at baseline									1.00 (1.36)	0.977

HR, hazard ratio; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA_{1c}, Haemoglobin A1c; LDL-C, low-density lipoprotein cholesterol; TG, triacylglycerol; HDL-C, high-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; ACR, urinary albumin to creatinine ratio; rLTL, relative leucocyte telomere length calculated by negative control (water). Sex and retinopathy were included as strata variables.

Model 1: without adjustment

Model 2: adjusted for age and sex

Model 3: Model 2 + adjusted for duration of diabetes, BMI, SBP and DBP

Model 4: Model 3 + adjusted for HbA1c, LDL-C, \log_{10} (triacylglycerol), HDL-C, eGFR and \log_{10} (ACR)

Model 5: Model 4 + retinopathy, neuropathy and CVD at baseline.

ESM Table 7 Cox regression showing the association between rLTL calculated based on QC materials and incident end stage kidney disease.

Variables	Model 1		Model 2		Model 3		Model 4		Model 5	
	HR (95%CI)	<i>p value</i>	HR (95%CI)	<i>p value</i>	HR (95%CI)	<i>p value</i>	HR (95%CI)	<i>p value</i>	HR (95%CI)	<i>p value</i>
rLTL_QC, $\Delta\Delta Ct$	1.24 (1.16-1.34)	<0.001	1.17 (1.09-1.26)	<0.001	1.15 (1.07-1.24)	<0.001	1.13 (1.04-1.23)	0.003	1.14 (1.05-1.23)	0.002
Age, years			1.04 (1.03-1.04)	<0.001	1.02 (1.01-1.03)	<0.001	1.01 (1.00-1.02)	0.316	1.01 (0.99-1.02)	0.360
Diabetes duration, years					1.02 (1.01-1.04)	0.001	1.00 (0.99-1.02)	0.784	1.00 (0.99-1.02)	0.853
BMI, kg/m ²					1.02 (0.99-1.04)	0.179	0.99 (0.97-1.01)	0.427	0.99 (0.97-1.01)	0.435
SBP, mmHg					1.02 (1.01-1.03)	<0.001	1.01 (1.01-1.02)	<0.001	1.01 (1.01-1.02)	<0.001
DBP, mmHg					0.98 (0.97-0.99)	0.001	0.98 (0.97-0.99)	<0.001	0.98 (0.97-0.99)	<0.001
HbA _{1c} , mmol/mol							1.01 (1.01-1.02)	<0.001	1.01 (1.01-1.02)	<0.001
LDL-C, mmol/l							0.85 (0.78-0.94)	0.001	0.85 (0.77-0.93)	0.001
Log (TG)							1.43 (0.92-2.21)	0.108	1.48 (0.95-2.30)	0.080
HDL-C, mmol/l							1.22 (0.96-1.55)	0.109	1.23 (0.96-1.56)	0.096
eGFR, ml min ⁻¹ 1.73 m ⁻²							0.98 (0.97-0.98)	<0.001	0.98 (0.97-0.98)	<0.001
Log (ACR)							2.99 (2.60-3.44)	<0.001	2.94 (2.55-3.38)	<0.001
Neuropathy									1.20 (0.98-1.48)	0.078
CVD at baseline									0.88 (0.67-1.15)	0.337

HR, hazard ratio; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA_{1c}, Haemoglobin A_{1c}; LDL-C, low-density lipoprotein cholesterol; TG, triacylglycerol; HDL-C, high-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; ACR, urinary albumin to creatinine ratio; rLTL, relative leucocyte telomere length calculated by QC.

Sex and retinopathy were included as strata variables.

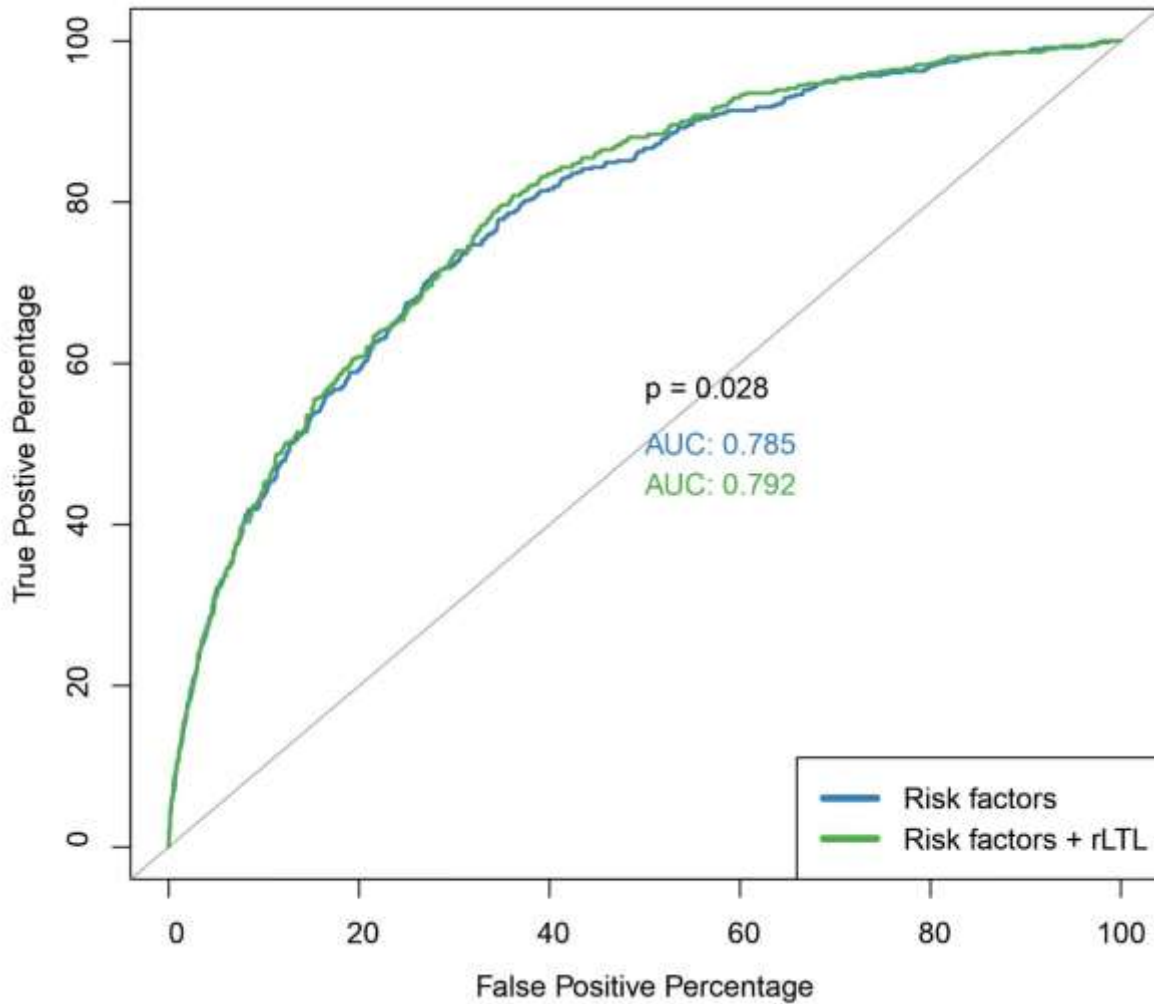
Model 1: without adjustment

Model 2: adjusted for age and sex

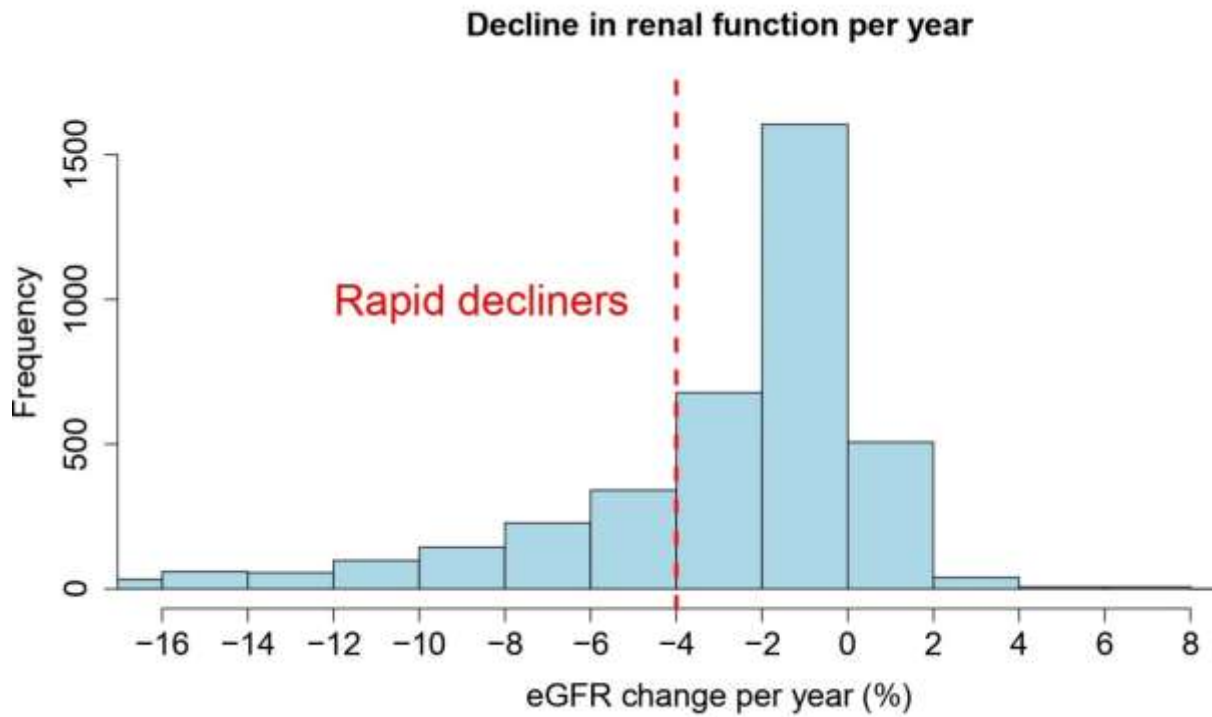
Model 3: Model 2 + adjusted for duration of diabetes, BMI, SBP and DBP

Model 4: Model 3 + adjusted for HbA1c, LDL-C, \log_{10} (triacylglycerol), HDL-C, eGFR and \log_{10} (ACR)

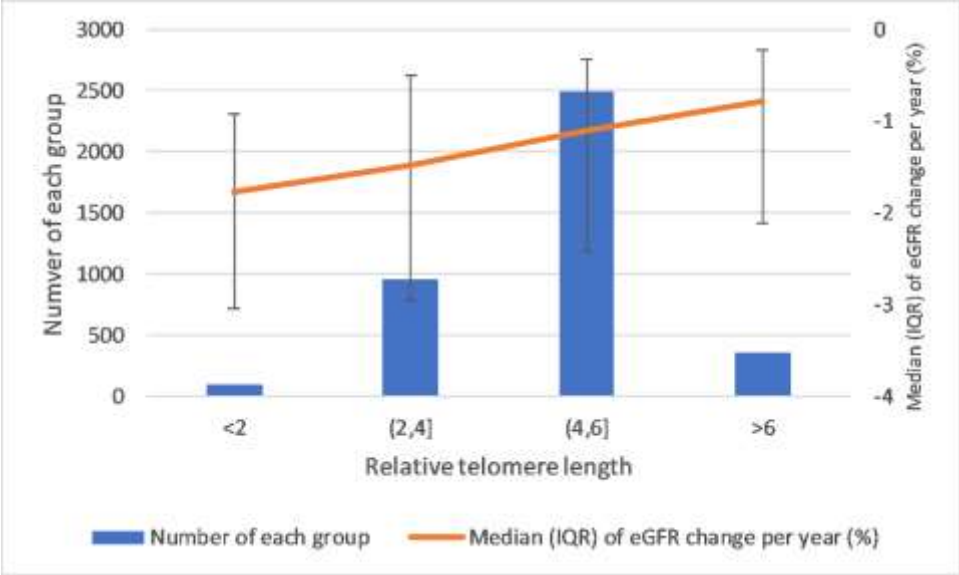
Model 5: Model 4 + retinopathy, neuropathy and CVD at baseline.



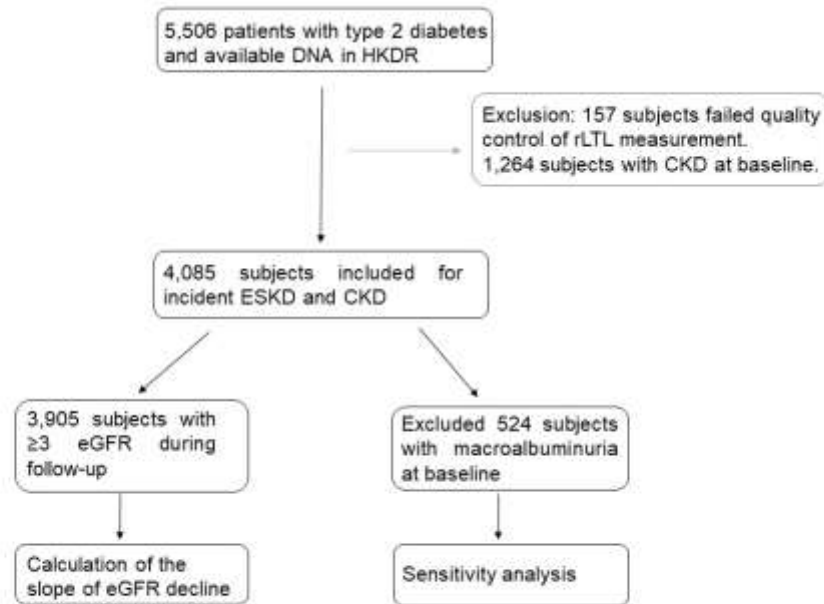
ESM Figure 1. Receiver operating characteristic curve (ROC) for prediction of end stage kidney disease. Traditional risk factors models with or without inclusion of rLTL (Area under the curve: 0.792 (0.772-0.813) vs. 0.785 (0.764-0.806), $P=0.002$). rLTL: relative leucocyte telomere length calculated by negative control (water).



ESM Figure 2. The histogram of decline in renal function per year during follow-up. Patients with eGFR decline of $>4\%/year$ were defined as rapid decliners.



ESM Figure 3. Association between rLTL at baseline and median (IQR) of eGFR change per year during the follow-up period.



ESM Figure 4. Flow diagram of patient selection

Abbreviation: HKDR, Hong Kong Diabetes Register; rLTL, relative leucocyte telomere length; CKD, chronic kidney disease; ESKD, end stage kidney disease; eGFR, estimated glomerular filtration rate